ELSEVIER

Carbohydrate Research 274 (1995) 123–136

CARBOHYDRATE
RESEARCH

Direct glycosylation of protected *O*-tritylserine esters and oligopeptides

Andrzej Rajca [a,*], Manfred Wiessler [b]

[a] *Institute of Organic Chemistry and Technology, Technical University of Silesia, Krzywoustego 4 Street, 44-101 Gliwice, Poland*

[b] *Department of Molecular Toxicology, German Cancer Research Center, Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany*

Received 4 August 1992; accepted in revised form 27 January 1995

Abstract

N-Fmoc-3-*O*-Tr-L-serine methyl and benzyl esters, as well as a tripeptide FmocAlaSer(Tr)GlyOBn were directly glycosylated by 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-galactopyranose in the presence of $TrClO_4$ in dichloromethane, yielding 32–57% of *N*-Fmoc-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-L-serine esters and the corresponding tripeptide.

Keywords: Glycosylation; *N*-9-Fluorenylmethoxycarbonyl-*O*-tritylserine esters; Serine glycosides; Serine glycopeptides; Cyanoethylidene condensation

---

1. Introduction

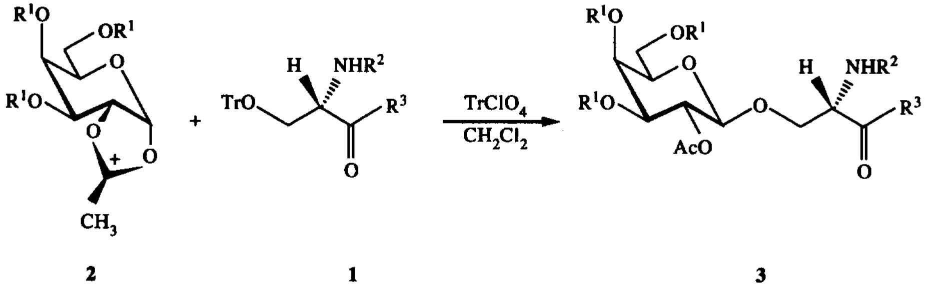
Recently, growing interest has been focused on the development of convenient methods for synthesising O-glycopeptides. These are partial structures of glycoproteins, which are important components of cell membranes. These glycoproteins play a key role in biological recognition processes, for example, the recognition of antigens by receptors, cell–cell communication, immunological response, or intracellular transport of proteins [1]. The progress in this field in the course of the last few years has been summarised in several reviews [2–9].

Two general strategies of synthesising O-glycopeptides have been used: the more common solid-phase or solution synthesis of the peptide chain with utilisation of

---

[*] Corresponding author.

SSDI 0008-6215(95)00097-6



R^1 = protecting group or protected fragment of carbohydrate group
R^2, R^3 = protecting group or protected fragments of the peptide chain

Scheme 1.

suitably protected *O*-glycosylated hydroxy amino acids as building-blocks of the peptide chain [2–5,10,11] or, rarely, the direct glycosylation of previously obtained oligopeptides [12–15] as occurs in the natural synthesis of O-glycoproteins.

In the synthesis of *O*-glycosylated hydroxy amino acids modern variants of the Koenigs–Knorr [2–5,10,16–18], trichloracetimidate [5,6,17,19–21], or thioglycoside methods [2,22–24] are commonly used.

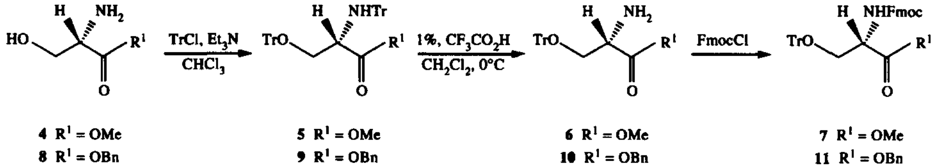
One of the reactions, potentially of value in both strategies, is the glycosylation of trityl ethers of protected hydroxy amino acids or their protected oligopeptides **1** with acyloxonium cations **2** formed in situ from suitably protected glycosyl donors (Scheme 1).

We now report the application of this reaction to the synthesis of protected serine glycosides and the direct glycosylation of protected trityl ethers of serine oligopeptides.

The use of trityl ethers in glycoside synthesis has a long tradition. The literature up to the late seventies has been reviewed by Bochkov and Zaikov [25]. Selective tritylation of the primary hydroxyl group, followed by complete acylation or benzylation of the remaining hydroxyl groups, and final acidolytic detritylation leads to derivatives with a selectively deprotected primary hydroxyl group. These have been widely used as glycosyl acceptors in numerous disaccharide syntheses to give (1 → 6)-linked D-glucose, D-galactose, and D-mannose, and (1 → 5)-linked L-arabinofuranose [25].

Bredereck et al. [26] observed that acyl cations react directly with trityl ethers of primary carbohydrate hydroxyl groups with cleavage of the ether bond. They employed this reaction in glycosylation and obtained disaccharides in good yield [27–29]. The same key stage was accomplished by Kochetkov and co-workers in the synthesis of di-, oligo-, and poly-saccharides, starting with protected 1,2-*O*-(1-cyanoethylidene) monosaccharides as glycosyl donors and carbohydrate trityl ethers as glycosyl acceptors [30]. The results of Kochetkov's group have been reviewed in detail [31].

On the other hand, Barlos and co-workers have developed a convenient method of synthesising *N*-(9-fluorenylmethoxycarbonyl)-*O*-trityl hydroxy amino acids and their oligopeptides [32], which are convenient starting materials for the synthesis of O-glycopeptides. In such syntheses the choice of groups protecting the amino and carboxy



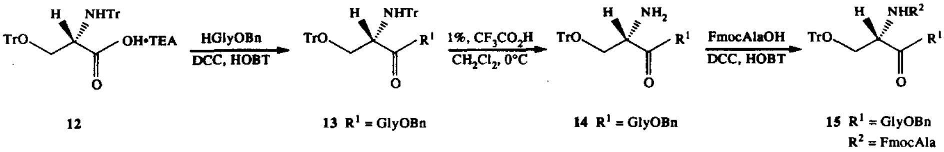
Scheme 2.

functions of amino acids or oligopeptides is especially important because they have to be removed without destroying the acid-sensitive glycosidic bond, or inducing base-catalysed β-elimination in serine or threonine derivatives. The problems of the proper selection of protecting groups for the glycopeptide synthesis have been discussed [2–5]. From this point of view the choice of the 9-fluorenylmethoxycarbonyl (Fmoc) group for temporary protection of the amino function is very convenient, because it can be removed under mild basic conditions by means of secondary amines such as piperidine or morpholine. Similarly the protection of carboxyl groups as benzyl esters, which are easily removable by catalytic hydrogenolysis, is also recommended [4].

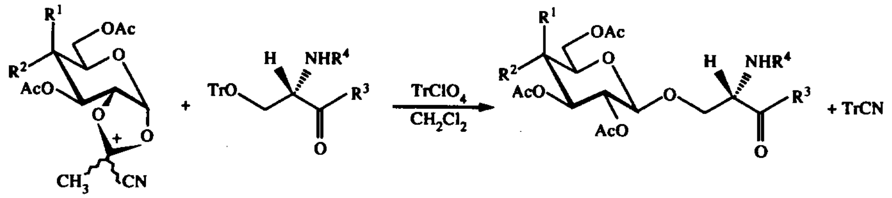
2. Results and discussion

Following Barlos at al. [32], we synthesised in a similar way new *N*-Fmoc-*O*-Tr-serine methyl and benzyl esters (**7** and **11**), as suitable starting materials for preliminary experiments in the glycosylation of serine trityl ethers (Scheme 2). Thus, the serine methyl and benzyl esters (**4** and **8**) were tritylated on both amino and side-chain hydroxyl functions. The resulting *N*,*O*-ditritylserine esters (**5** and **9**) were selectively detritylated at the α-amino group by 1% trifluoroacetic acid in dichloromethane, at 0°C in a few minutes. TLC revealed that under such conditions *N*-detritylation was incomplete, but on the other hand prolongation of the reaction time or using higher concentrations of trifluoroacetic acid causes undesired *O*-detritylation. The *N*-deprotected *O*-tritylserine esters **6** and **10** were readily acylated in high yield under classical Carpino conditions [33] to give the *N*-Fmoc-*O*-Tr derivatives **7** and **11**.

FmocAlaSer(Tr)GlyOBn (**15**), the model tripeptide used to check the possibility of direct glycosylation of protected *O*-tritylserine oligopeptides, was obtained according to a similar scheme (Scheme 3), where serine was incorporated into the peptide chain in excellent yield from the triethylamine salt **12** of the acid by means of the carbodiimide method with *N*-hydroxybenzotriazole (HOBT) as a promoter.



Scheme 3.



16a,b 17a,b **7, 11, 15** **18, 19, 20, 21**

Compound	R^1	R^2	Isomer
16a	AcO	H	exo
16b	AcO	H	endo
17a	H	Ac$_4$-β-D-Gal*p*-(1→4)-O	exo
17b	H	Ac$_4$-β-D-Gal*p*-(1→4)-O	endo

Compound	R^3	R^4
7	OMe	Fmoc
11	OBn	Fmoc
15	GlyOBn	FmocAla

Compound	R^1	R^2	R^3	R^4
18	AcO	H	OMe	Fmoc
19	AcO	H	OBn	Fmoc
20	AcO	H	GlyOBn	FmocAla
21	H	Ac$_4$-β-D-Gal*p*-(1→4)-O	OBn	Fmoc

Scheme 4.

The resulting dipeptide ester **13** was selectively *N*-detritylated as described above, and the *N*-deprotected dipeptide **14** condensed with FmocAlaOH, similarly to *N,O*-ditritylserine. Owing to the high reactivity of the *N*-hydroxybenzotriazolyl esters of the amino acids formed in situ, the yields of compounds **13** and **15** were high (> 85%).

For experiments on the direct glycosylation of the protected trityl ethers of serine (**7** and **11**) we selected the Bochkov and Kochetkov variant for the generation of dioxolenium cations **2**, starting from the well-characterised 1,2-cyanoethylidene carbohydrate derivative **16a** and **b** [34] and trityl perchlorate as catalyst [30] (Scheme 4). The reaction of compounds **7** and **11** with 3,4,6-tri-*O*-acetyl-1,2-*O*-[(*exo* and *endo*)-1-cyanoethylidene]-D-galactopyranose [1] (**16a,b**), performed under conditions similar to the Kochetkov synthesis of disaccharides, in dichloromethane, with 0.05–0.1 mole $TrClO_4$ as a catalyst for 1 mole of substrates, gave the expected β-glycosides in a low yield of 35% (**18**) and 32% (**19**), respectively. The structure of both products was confirmed by MS, and by ^1H and ^{13}C NMR spectra.

We have also shown that the protected serine tripeptide **15** is a suitable glycosyl acceptor in this reaction. The glycosylation of this tripeptide under Kochetkov's conditions gave the β-glycoside **20** with a yield of 37%, better than in the glycosylation of compounds **7** and **11**.

Similarly, in the reaction of hepta-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)lactose (mixture of *exo* and *endo* isomers, **17a** and **17b**) with *N*-FmocSer(Tr)OBn (**11**) we obtained a low yield (20%) of *N*-9-fluorenylmethoxycarbonyl-*O*-[2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-L-serine benzyl ester (**21**).

---

[1] *exo* and *endo* refer to the methyl group [34], and correspond to *R* and *S* configurations, respectively.

In the case of glycosyl donors bearing participating groups like OAc or OBz in the neighbourhood of the anomeric centre, which could form acyloxonium cations of type **2** such as **22** and **23** (Scheme 5), the expected glycosylation products are 1,2-*trans*(here β)-glycosides **18–21**, because nucleophilic attack of the trityl ether on C-1 takes place from the rearside to the C–O linkage. Nevertheless the formation of α anomers **24–27** in amounts varying between 0 to 50% of the yield in other similar systems has been observed [31].

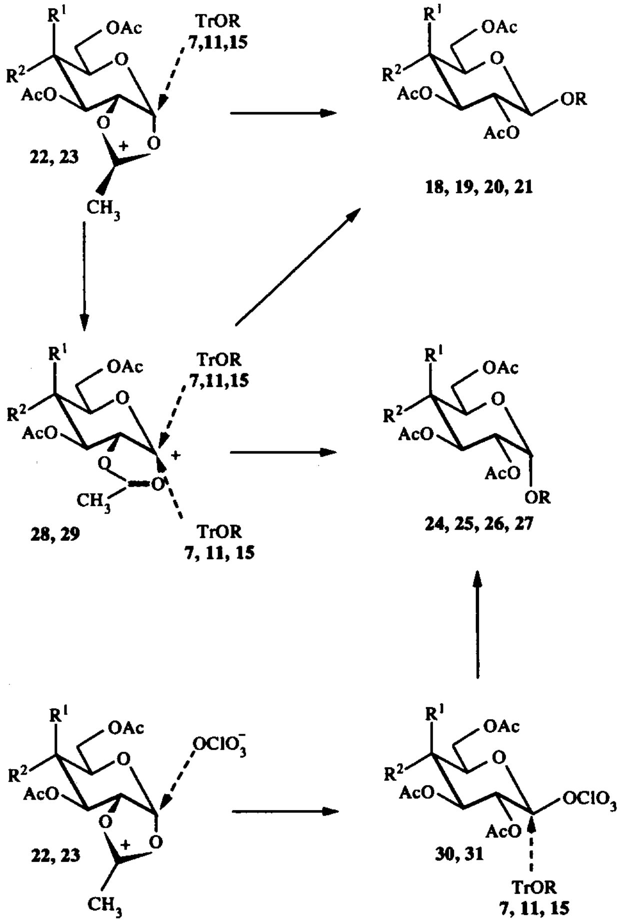
The stereoselectivity of this reaction is strongly dependent on the structure of the trityl ether, on the nature of the initiator, or more precisely on the tritylium salt anion, and on the pressure in the reaction system [31]. The formation of *cis*-glycosides **24–27** (see Scheme 5) could be explained by transforming the dioxolenium bicyclic cations **22** or **23** into monocyclic glycosyl cations **28, 29** which are open to nucleophilic attack from both sides. Another possibility is a nucleophilic attack of the perchlorate anion, followed by its second substitution by trityl ether [31].

In our experiments we have isolated β-glycosides as the main products, but also other fractions, in very low yield, which on the basis of their ^{1}H NMR and UV spectra, as well as TLC colour test reactions, contained both Fmoc and carbohydrate units. They were not pure enough for conclusive identification, but from their amounts we can conclude that the ratio between β- and α-glycosides was better than 4:1.

The low yields and low rates of the reaction prompted us to test its optimisation. Experiments were performed on the scale of several milligrams using as an example the reaction of FmocSer(Tr)OBn (**11**) and the glycosyl donor **16a,b**, in the presence of $TrClO_4$ as the catalyst, and followed by an HPLC method especially designed for this purpose. The experiments showed that according to the conditions proposed for disaccharide syntheses [30] the reaction is very slow and is incomplete after several hours. The reactivity of serine trityl ethers is essentially lower than the reactivity of 6-trityl ethers of carbohydrate derivatives. To improve the yield and reaction rate, we tested the influence of the ratio between the catalyst (tritylium perchlorate) and substrates on the yield of glycoside **19**. The results are presented in Fig. 1. The initial reaction rates are strongly dependent on the concentrations of the catalyst. The highest yields of the main product, more than 60% [by conversion of the starting material FmocSer(Tr)OBn, 85%], were observed with an almost stoichiometric amount of the catalyst after 5 h. However, lower amounts of the catalyst, between 0.25–0.5 mole for 1 mole of substrates, also gave yields above 50%, but after a longer time. In the case of stoichiometric amounts of the catalyst we observed a diminishing yield with longer reaction times, revealing a contribution of further reactions.

One of the side reactions in this system is the formation of *O*-acetyl-*N*-(9-fluorenylmethoxycarbonyl)-L-serine benzyl ester [FmocSer(Ac)OBn, **32**]. We have isolated this compound in 20% yield from the reaction mixture, and identified it from its ^{1}H NMR, mass, and UV spectra. Formation of a similar product of acylation of the aglycon was observed earlier by Banoub and Bundle [35,36].

Preparative results were in good agreement with the small-scale observations. Deduced from Fig. 1 the initial reaction rates for 5–10 mol% of catalyst lead to the conclusion that after several hours the yield of the product should be ca. 30–40%, as we had found.



Compound	R	R^1	R^2
7	- $CH_2CH(NHFmoc)COOMe$	–	–
11	- $CH_2CH(NHFmoc)COOBn$	–	–
15	- $CH_2CH(NHCOCH(CH_3)NHFmoc)CONHCH_2COOBn$	–	–
18, 24	- $CH_2CH(NHFmoc)COOMe$	AcO	H
19, 25	- $CH_2CH(NHFmoc)COOBn$	AcO	H
21, 27	- $CH_2CH(NHFmoc)COOBn$	H	Ac_4-β-D-Gal*p*-(1→4)-O
20, 26	- $CH_2CH(NHCOCH(CH_3)NHFmoc)CONHCH_2COOBn$	AcO	H
22, 28, 30	–	AcO	H
23, 29, 31	–	H	Ac_4-β-D-Gal*p*-(1→4)-O

Scheme 5. Formation of α- and β-glycosides in the reaction of trityl ethers and dioxolenium cations (according to ref. [31]).

A preparative experiment under optimised conditions gave an isolated yield of 57% of compound **19**, and 47% of compound **21**, dependent on the quality of the chromatographic separation. HPLC analysis revealed other limitations of these reactions. In the

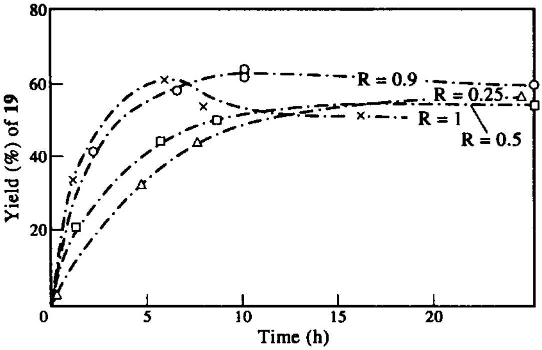
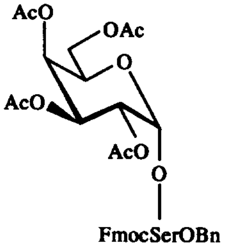
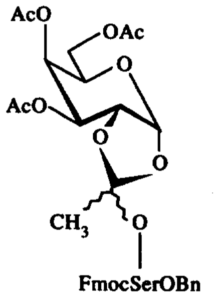


Fig. 1. The influence of the ratio (R) between substrate FmocSer(Tr)OBn **11** and catalyst $TrClO_4$ on the yield of FmocSer(Ac_4-β-D-Gal*p*)OBn **19** (molar ratio between **11** and **16a,b** = 1).

reaction mixture we observed three other side-products containing the fluorenyl moiety. One of them was *N*-FmocSer(H)OBn, formed from FmocSer(Tr)OBn under the influence of trityl perchlorate after hydrolysis in the analytical system. Two others, on the basis of their ^1H NMR spectra, were recognised as the α-glycoside **25** and probably the ortho-ester **33a,b** (mixture of *exo* and *endo* forms, signal of ortho-ester Me group, δ ca. 1.64). However, they were isolated in small amounts and were not pure enough for conclusive identification. Formation of ortho-esters was also observed by Polt et al. [18] in a similar reaction.



25



33a, b

The conclusion is that one should not expect yields of the main product higher than 60–70% in this reaction system. The advantage of this approach in comparison with other established methods is the direct reaction of protected serine derivatives and oligopeptides, without deprotection and purification of *O*-deprotected derivatives. The direct glycosylation of resin-bound peptides has also been shown to be possible [15,37]; however, it offers lower yields compared to the building block strategy [37] and needs optimisation to be the method of choice.

3. Experimental

General methods.—Serine methyl and benzyl esters, FmocCl, and HOBT were commercial products from Serva (Heidelberg, Germany), FmocAlaOH was from Bachem Feinchemical AG (Bubendorf, Switzerland), and L-serine benzyl ester from Sigma (Deisenhofen, Germany). The melting points were determined with an apparatus according to Dr Tottoli and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on Tesla 80, Bruker 90, and Bruker 250 MHz spectrometers in $CDCl_3$ (if not specified otherwise), EI-MS spectra were run on an MAT-11 mass spectrometer (Institute of Biochemistry of the German Cancer Research Center, Heidelberg, Germany). The specific rotations were measured on a Perkin–Elmer type 241 polarimeter (Institute of Biochemistry II, Heidelberg University, Germany). Column chromatography was carried out on Kieselgel 60 (240–400 mesh) from E. Merck, Darmstadt, Germany, and monitored by TLC on DC sheets Kieselgel 60 F_{254} from E. Merck. Preparative TLC was carried out on Kieselgel 60 F_{254} precoated sheets from E. Merck. The components were detected by UV light (compounds containing Fmoc moiety), or by spraying with concd H_2SO_4 containing 1% of vanillin (Tr-containing components gave yellow spots immediately after contact with H_2SO_4; carbohydrate derivatives were visualised as black stains after heating in a stream of hot air). HPLC was carried out on the Hewlett–Packard 1090-LC system using an RP-18-5μ 250 + 4.6 mm column; flow, 1.5 mL/min; linear gradient from 1:1 CH_3CN–H_2O to 100% CH_3CN in 50 min; detection $\lambda = 300$ nm (for Fmoc-containing components). Methylene chloride used as a solvent for glycosylation was carefully dried by boiling for several hours over CaH_2 and distilled from CaH_2 into a reaction flask immediately before the reaction.

N,O*-Ditrityl-*L*-serine methyl ester* (**5**).—This compound was obtained in a similar way to Dijkman et al. [38]. To L-serine methyl ester (**4**) hydrochloride (1.56 g, 10 mmol) in $CHCl_3$ (20 mL) was added triethylamine (TEA) (3.58 g, 4.92 mL, 35 mmol), followed by trityl chloride (5.57 g, 20 mmol), added in two portions. The mixture, protected by a $CaCl_2$ tube, was cooled during the first exothermic period of the reaction and stirred for 17 h, then it was dissolved in $CHCl_3$, washed with water, dried over $CaCl_2$, and evaporated. The residue was evaporated twice with EtOH. After the addition of EtOH (30 mL), crystallisation occurred to yield **5** (3.2 g, 53%); mp 130–135°C (from EtOH); ^{1}H NMR (80 MHz): δ 7.8–7.13 (m, 31 H, 2 Tr, NH), 3.8–3.3 (m, 3 H, 2 Hβ-Ser, Hα-Ser), 3.2 (s, 3 H, OMe).

O*-Trityl-*L*-serine methyl ester* (**6**).—To 20 mL of 1% CF_3CO_2H in CH_2Cl_2, cooled in an ice-bath, was added **5** (0.5 g, 0.83 mmol). The mixture was stirred for 3 min and the solvents were evaporated at low temperature. The residue, dissolved in $CHCl_3$, was washed with aq 5% $NaHCO_3$ and water, dried over Na_2SO_4, and chromatographed on silica gel to give **6** as an oil (125 mg, 41%); ^{1}H NMR (80 MHz): δ 7.6–7.18 (m, 15 H, Tr), 3.7 (s, 3 H, OMe), 3.68–3.15 (m, 3 H, 2 Hβ-Ser, Hα-Ser), 1.98 (s, 2 H, NH_2).

N*-9-Fluorenylmethoxycarbonyl-*O*-trityl-*L*-serine methyl ester* (**7**).—To **6** (121 mg, 0.335 mmol) in 1,4-dioxane (8 mL) and aq 10% Na_2CO_3 (10 mL) was added dropwise a solution of 9-fluorenylmethoxycarbonyl chloride (87 mg, 0.335 mmol) in 1,4-dioxane (3 mL), while being stirred and cooled in an ice-bath. The mixture was stirred for 1.5 h at the temperature of the ice-bath and for 15 h at room temperature. Then EtOAc (30 mL) and water (30 mL) were added, and the water phase was extracted 3 times with EtOAc (10 mL). The combined organic extracts were washed with aq 1% citric acid, aq 5% $NaHCO_3$, and water, dried, and evaporated. The residue was chromatographed on silica gel to yield **7** (114 mg, 69%) as an oil; $[\alpha]_D^{20}$ + 3.6° (*c* 2, $CHCl_3$); ^{1}H NMR (80 MHz): δ 7.8–7.15 (m, 23 H, Tr, Ar-Fmoc), 5.7 (d, 1 H, NH), 4.7–4.0 (m, 4 H, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}$-Fmoc, H$\alpha$-Ser), 3.75 (s, 3 H, OMe), 3.6–3.3 (m, 2 H, 2 Hβ-Ser). Anal. Calcd for $C_{38}H_{33}NO_5$: C, 78.20; H, 5.70; N, 2.40. Found: C, 78.35; H, 5.49; N, 2.21.

N,O-*Ditrityl*-L-*serine benzyl ester* (**9**).—L-Serine benzyl ester (**8**) hydrochloride (1.16 g, 5 mmol), trityl chloride (3.6 g, 11 mmol), and TEA (1.61 g, 2.22 mL, 16 mmol) in CH_2Cl_2 (15 mL) were stirred for 24 h. Then CH_2Cl_2 (50 mL) was added, and the solution was washed with water, dried over $CaCl_2$, and evaporated. The oily residue was boiled with EtOH (40 mL) to give solid **9** (3.2 g, 94%); mp 156–157°C (from EtOH); ^{1}H NMR (250 MHz): δ 7.50–7.10 (m, 35 H, Tr, $\mathrm{CH}_2\mathit{Ph}$), 4.67 (d, 1 H, $\mathrm{C}\mathit{H}_\mathrm{a}\mathrm{H}_\mathrm{b}\mathrm{Ph}$), 4.45 (d, 1 H, $\mathrm{CH}_\mathrm{a}\mathit{H}_\mathrm{b}\mathrm{Ph}$), 3.59 (m, 1 H, H$\alpha$-Ser), 3.43 (dd, 1 H, H$\beta$a-Ser), 3.33 (dd, 1 H, H$\beta$b-Ser), 2.86 (d, 1 H, NH); $J_{\mathrm{Ha,Hb}}$ 12.4, $J_{\mathrm{H}\alpha,\mathrm{H}\beta\mathrm{a}}$ 4.7, $J_{\mathrm{H}\alpha,\mathrm{H}\beta\mathrm{b}}$ 6.6, $J_{\mathrm{H}\beta\mathrm{a},\mathrm{H}\beta\mathrm{b}}$ 8.6, $J_{\mathrm{NH,CH}\alpha}$ 10.4 Hz. Anal. Calcd for $C_{48}H_{41}NO_3$: C, 84.80; H, 6.08; N, 2.06. Found: C, 84.54; H, 6.21; N, 2.17.

O-*Trityl*-L-*serine benzyl ester* (**10**).—To **9** (1 g, 1.47 mmol), dissolved in CH_2Cl_2 (50 mL) and cooled to 0°C, was added CF_3CO_2H (0.3 mL). After 5 min, the solvent and excess of CF_3CO_2H were evaporated at a low temperature, the residue was dissolved in MeOH and evaporated, and a solution of the residue in EtOAc was washed with aq 5% $NaHCO_3$ and H_2O, dried over Na_2SO_4, and chromatographed on silica gel, to yield **10** as an oil [665 mg (the product contained one molecule of eluent acetone), 91%]. ^{1}H NMR (80 MHz): δ 7.7–7.1 (m, 20 H, Tr, $\mathrm{CH}_2\mathit{Ph}$), 5.2 (s, 2 H, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 3.8–3.3 (m, 3 H, 2 H$\beta$-Ser, H$\alpha$-Ser), 2.08 (s, 6 H, CH_3COCH_3), 1.8 (s, 2 H, NH_2).

N-*9-Fluorenylmethoxycarbonyl*-O-*trityl*-L-*serine benzyl ester* (**11**).—To **10** (600 mg, 1.37 mmol) in 1,4-dioxane (6 mL) and aq 10% Na_2CO_3 (10 mL), cooled to 0°C, was added dropwise a solution of FmocCl (355 mg, 1.37 mmol) in 1,4-dioxane (10 mL). The mixture was stirred for 1 h at 0°C and 12 h at room temperature. Water (30 mL) and EtOAc (30 mL) were added, the water phase was extracted 3 times with EtOAc, the combined organic extracts were washed with aq 2% citric acid, aq 5% $NaHCO_3$, and water, then dried over Na_2SO_4 and evaporated to give **11** as a solidifying foam (884 mg, 98%); mp 69–73°C (crude product); $[\alpha]_D^{20}$ + 1.2° (*c* 2, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.82–7.20 (m, 28 H, Tr, $\mathrm{CH}_2\mathit{Ph}$, Ar-Fmoc), 5.75 (d, 1 H, NH), 5.24 (AB, 2 H, $\mathrm{C}\mathit{H}_\mathrm{a}\mathit{H}_\mathrm{b}\mathrm{Ph}$), 4.54 (dt, 1 H, H$\alpha$-Ser), 4.45–4.15 (m, 3 H, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}$-Fmoc), 3.62 (dd 1 H, H$\beta$a-Ser), 3.43 (dd, 1 H, H$\beta$b-Ser); $J_{\mathit{H}\mathrm{a}\mathit{H}\mathrm{bPh}}$ 12, $J_{\mathrm{H}\alpha,\mathrm{H}\beta\mathrm{a}}$ 4.6, $J_{\mathrm{H}\alpha,\mathrm{H}\beta\mathrm{b}}$ 4 Hz, $J_{\mathrm{H}\beta\mathrm{a},\mathrm{H}\beta\mathrm{b}}$ 8.7, $J_{\mathrm{NH,H}\alpha}$ 8.2 Hz. Anal. Calcd for $C_{44}H_{37}NO_5$: C, 80.10; H, 5.65; N, 2.12. Found: C, 80.23; H, 5.76; N, 2.27.

N-*Trityl*-L-*serine triethylamine salt*.—This was synthesised according to Barlos at al. [39] (prescription for *N*-tritylthreonine, Procedure C), 76% yield.

N,O-*Ditrityl*-L-*serine triethylamine salt* (**12**).—The sodium salt of TrSer(Tr)OH was obtained from TrSer(H)OH · TEA according to Barlos and co-workers [32,39], transformed into the triethylamine salt, and then purified by column chromatography on silica gel to give **12** as a solidifying foam; ^{1}H NMR (80 MHz): δ 7.9–6.9 (m, 31 H, 2 Tr, NH), 3.3 (broad s, 3 H, 2 Hβ-Ser, Hα-Ser), 2.6 (q, 6 H, 3 CH_2-TEA), 0.9 (t, 9 H, 3 CH_3-TEA).

*N,O-Ditrityl-*L*-serylglycine benzyl ester* (**13**).—The TEA salt **12** (924 mg 1.57 mmol) and TSA · HGlyOBn (530 mg, 1.57 mmol) in CH_2Cl_2 (7 mL) were coupled with dicyclohexylcarbodiimide (DCC) (323 mg, 1.57 mmol) in the presence of *N*-hydroxybenzotriazole (HOBT) (300 mg, 2.22 mmol) according to the standard procedure, to give **13** as a solidifying foam (1.144 g, 99%); ^{1}H NMR (80 MHz): δ 7.7–7 (m, 36 H, 2 Tr, CH_2*Ph*, NH), 5.2 (s, 2 H, CH_2Ph), 3.8 (d, 2 H, 2 Hα-Gly), 3.8–2.7 (m, 4 H, 2 Hβ-Ser, Hα-Ser, NH).

*O-Trityl-*L*-serylglycine benzyl ester* (**14**).—TrSer(Tr)GlyOBn **13** (1.144 g, 1.57 mmol) in CH_2Cl_2 (30 mL) was cooled to 0°C and CF_3CO_2H (0.3 mL) was added. After 10 min, the solvents and excess of CF_3CO_2H were evaporated, the residue was dissolved in EtOAc (50 mL), and the solution washed with aq 5% $NaHCO_3$ and water, then dried and evaporated. The residue was chromatographed on silica gel, to give **14** as an oil (481 mg, 63%); ^{1}H NMR (80 MHz): δ 8.0–7.0 (m, 20 H, Tr, CH_2*Ph*), 5.1 (s, 2 H, CH_2Ph), 4.45–3.85 (m, 3 H, 2 Hα-Gly, NH), 3.6–3.2 (m, 3 H, 2 Hβ-Ser, Hα-Ser), 2.1 (s, 2 H, NH_2).

*N-9-Fluorenylmethoxycarbonyl-*L*-alanyl-O-trityl-*L*-serylglycine benzyl ester* (**15**).—HSer(Tr)GlyOBn **14** (386 mg, 0.78 mmol) and Fmoc-L-AlaOH (243 mg, 0.78 mmol) in CH_2Cl_2 (6 mL) were coupled with DDC (161 mg, 0.78 mmol) in the presence of HOBT (180 mg, 1.18 mmol) for 2 h at −10°C and then for 14 h at room temperature. After standard work-up a solid (575 mg) was obtained, and purified by column chromatography on silica gel to give **15** (534 mg, 87%); $[\alpha]_D^{20}$ + 5.7° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.78–7.10 (m, 29 H, Tr, Ar-Fmoc, CH_2*Ph*, NH), 6.68 (d, 1 H, NH), 5.20 (t, 1 H, NH-Gly), 5.16 (s, 2 H, CH_2Ph), 4.55 (m, 1 H, Hα-Ala), 4.43 (dd, 1 H, Hα-Ser), 4.30–4.20 (m, 2 H, CH_2-Fmoc), 4.12 (pseudo-t, 2 H, 2 Hα-Gly), 3.93 (dd, 1 H, Hβa-Ser), 3.70 (dd, 1 H, CH-Fmoc), 3.22 (dd, 1 H, Hβb-Ser), 1.62 (d, 3 H, Hβ-Ala).

*3,4,6-Tri-O-acetyl-1,2-O-[(*exo *and* endo*)-1-cyanoethylidene]-α-*D*-galactopyranose* (**16a,b**).—This was synthesised according to ref [34] as a mixture of *exo* and *endo* isomers (83%).

*3,6-Di-O-acetyl-1,2-O-[(*exo *and* endo*)-1-cyanoethylidene]-4-O-(2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl)-α-*D*-glucopyranose* (**17a,b**).—Hepta-*O*-acetyl-α-lactosyl bromide (1.924 g, 2.75 mmol), KCN (1.63 g, 25 mmol), and $(n\text{-Bu})_4NBr$ (750 mg, 2.3 mmol) in dry MeCN (15 mL) were stirred at 20°C for 20 h, then diluted with EtOAc (150 mL), washed with water (7 × 50 mL), and dried over Na_2SO_4. Solvents were evaporated, the residue was dissolved in $CHCl_3$ (5 mL), the solution was filtered through a 3-cm layer of silica gel [elution with 1:2 $CHCl_3$–petroleum ether (100 mL)] and concentrated, and the residue was chromatographed on silica gel to yield 854 mg (48%) of an oily mixture of *exo* and *endo* isomers (δ CMe groups in ^{1}H NMR: 1.92 for *endo* and 1.75 for *exo* isomers). After additional chromatography on silica gel the pure *endo* isomer **17b** was obtained (330 mg, 19%); ^{1}H NMR (250 MHz): δ 5.75 (d, 1 H, H-1), 5.62 (dd, 1 H, H-3), 5.38 (dd, 1 H, H-4′). 5.17 (dd, 1 H, H-2′), 5.00 (dd, 1 H, H-3′), 4.60 (d, 1 H, H-1′), 4.39 (ddd, 1 H, H-2), 4.20 (dd, 1 H, H-6a), 4.18–4.04 (m, 3 H, H-6a′, H-6b′, H-6b), 3.96 (dt, 1 H, H-5′), 3.78 (ddd, 1 H, H-5), 3.63 (dt, 1 H, H-4), 2.17–1.97 (6 s, 18 H, 6 Ac), 1.92 (s, 3 H, CMe); for galactose ring: $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.5,

$J_{3',4'}$ 3.5, $J_{4',5'}$ 1.2, $J_{5',6a'}$ 6.5, $J_{5',6b'}$ 6.5, $J_{6a',6b'}$ 12 Hz; for glucose ring:$J_{1,2}$ 5.1, $J_{2,3}$ 2.8, $J_{2,4}$ 1.1, $J_{3,4}$ 1.2, $J_{4.5}$ 9.4, $J_{5,6a}$ 2.4, $J_{5,6b}$ 5.6, $J_{6a,6b}$ 12 Hz; ^{13}C NMR: δ 170.5, 170.4, 170.2, 170.0, 169.4, 163.2 (6 ester C=O), 116.5 (CN), 102.7 (C-1'), 99.2 (*C*Me), 97.2 (C-1), 77.2, 74.0, 71.0, 70.9, 69.0, 68.9, 67.4, 66.8 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 63.1, 60.9 (C-6, C-6'), 24.2 (C*Me*), 20.8, 20.7, 20.64, 20.62, 20.53 (6 CO*Me*).

N-*9-Fluorenylmethoxycarbonyl-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-*L*-serine methyl ester* (**18**).—FmocSer(Tr)OMe **7** (114 mg, 0.195 mmol) and 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-galactose (**16a,b**) (60 mg, 0.21 mmol) were dissolved in CH_2Cl_2 and evaporated. The residue was dried for about 1 h under vacuum. Dichloromethane (ca. 8 mL), boiled over CaH_2, was distilled into the residue, followed by the addition of $TrClO_4$ (8 mg). The mixture was left for 16 h at room temperature, protected against contact with traces of water. Then 1:1 MeOH–pyridine (1 mL) was added, followed by CH_2Cl_2 (30 mL), the mixture was washed with water, dried over Na_2SO_4, and evaporated, and the residue was dissolved in CH_2Cl_2 and chromatographed on Kieselgel to yield **18** (35%) as an oil; TLC:R_f 0.48 (1:1 hexane–acetone); HPLC t_R 10.1 min; $[\alpha]_D^{20}$ +5.5° (*c* 1, $CHCl_3$) MS(EI): M^+ 671; calcd 671. Fragmentation: *m/z* 612, 475, 390, 331, 179, 178(B), 165, 130, 115, 102, 81, 43, 28, 18. ^{1}H NMR (250 MHz): δ 7.83–7.33 (dd + m, 8 H, Ar-Fmoc), 5.57 (d, 1 H, NH), 5.37 (dd, 1 H, H-4), 5.16 (dd, 1 H, H-2), 4.99 (dd, 1 H, H-3), 4.72–4.38 (m, 3 H, CH_2CH-Fmoc), 4.42 (d, 1 H, H-1), 4.30–4.20 (m, 2 H, Hα-Ser and Hβa-Ser), 4.13 (d, 2 H, H-6a, H-6b), 3.91–3.80 (m, 2 H, Hβb-Ser, H-5), 3.77 (s, 3 H, OMe), 2.14–1.94 (4 s, 12 H, 4 Ac); $J_{1,2}$ 7.9, $J_{2,3}$ 10.5, $J_{3,4}$ 3.4, $J_{4,5}$ 1.2, $J_{5,6a} = J_{5,6b}$ = 6.5 Hz; ^{13}C NMR: δ 170.3, 170,1, 170.0, 169.9, 169.3 (5 ester CO), 155.7 (NHCOO), 143.7, 143.5, 141.2 (4 aromatic quaternary carbons–Fmoc), 127.7, 127.0, 124.9, 120.0 (8 aromatic tertiary carbons–Fmoc), 101.6 (C-1), 70.7, 70.6 (C-3, C-5), 69.4 (Cβ-Ser), 66.9, 66.8 (*C*H_2-Fmoc, C-2), 64.5 (C-4), 61.1 (C-6), 54.2 (Cα-Ser), 52.7 (OMe), 47.1 (*C*H-Fmoc), 20.5, 20.47 (4 C*Me*). Anal. Calcd for $C_{33}H_{37}NO_{14}$: C, 59.01; H, 5.55; N, 2.09. Found: C, 58.89; H, 5.67; N, 2.01.

N-*9-Fluorenylmethoxycarbonyl-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-*L*-serine benzyl ester* (**19**).—It was synthesised like **18** from **11** and **16a,b**: (*a*) molar ratios **11**:**16a,b**:$TrClO_4$ = 1:1:0.3, reaction time 16 h, yield 32%,; (*b*) molar ratios **11**:**16a,b**:$TrClO_4$ = 1:1:1, reaction time 16 h, yield 53%,; (*c*) molar ratios **11**:**16a,b**:$TrClO_4$ = 1:1:1, reaction time 5 h, yield 57%. Compound **19** was an oil; $[\alpha]_D^{20}$ −1.2° (*c* 1, $CHCl_3$); TLC:R_f 0.34 (1:1 hexane–EtOAc); HPLC: t_R 16.5 min MS(EI): M^+ 747.2502; calcd for $C_{39}H_{41}NO_{14}$ 747.2527. Fragmentation: *m/z* 703, 557, 491, 428, 390, 331, 196, 179, 178(base), 165, 151, 91, 89, 43, 18. ^{1}H NMR (250 MHz): δ 7.78–7.25 (m, 13 H, Ar-Fmoc, CH_2*Ph*), 5.62 (d, 1 H, NH-Ser), 5.36 (dd, 1 H, H-4), 5.20 (s, 2 H, C*H*$_2$Ph), 5.17 (dd, 1 H, H-2), 4.98 (dd, 1 H, H-3), 4.41 (d, 1 H, H-1), 4.55–4.27 (m, 4 H, C*H*$_2$C*H*-Fmoc, Hα-Ser), 4.22 (t, 1 H, Hβa-Ser), 4.11 (d, 2 H, H-6a, H-6b), 3.91–3.78 (m, 2 H, Hβb-Ser, H-5), 2.14–1.98 (4 s, 12 H, 4 Ac); $J_{1,2}$ 7.8, $J_{2,3}$ 10.5, $J_{3,4}$ 3.4,$J_{4,5}$ 1.9, $J_{5,6a} = J_{5,6b}$ = 6.9 Hz; ^{13}C NMR: δ 170.3, 170.1, 170.0, 169.4 (5 ester C = O), 155.8 (NHCOO), 143.8, 143.6, 141.3 (4 quaternary aromatic carbons–Fmoc), 135.1 (quaternary aromatic carbon–CH_2Ph), 128.6, 128.1, 127.7, 125.0, 124.9, 120.0 (13 aromatic tertiary carbons), 101.6 (C-1), 70.8, 70.7 (C-3, C-5), 69.5 (Cβ-Ser), 68.6 (C-2), 67.6 (*C*H_2-Fmoc) 66.9 (*C*H_2Ph), 66.8 (C-4), 61.1 (C-6), 54.4 (Cα-Ser), 47.1 (*C*H-Fmoc), 20.6, 20.55, 20.53 (4 C*Me*). Anal. Calcd for $C_{39}H_{41}NO_{14}$: C, 62.65; H, 5.53; N, 1.87. Found: C, 62.53; H, 5.66; N, 1.74.

*N-9-Fluorenylmethoxycarbonyl-*L*-alanyl-O-(2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl)-*L*-serylglycine benzyl ester* (**20**).—Ester **20** was obtained, according to a procedure similar to that for the serine glycosides **18** and **19**, from **15** and **16a,b** and isolated by column chromatography, followed by preparative TLC, to yield **20** as an oil (37%); $[\alpha]_D^{20}$ −2.8° (*c* 1, $CHCl_3$); TLC:R_f 0.43 (5:1 $CHCl_3$–acetone); ^{1}H NMR (250 MHz): δ 7.8–7.27 (m, 13 H Ar-Fmoc, CH_2*Ph*), 7.06 (t, 1 H, NH-Gly), 6.86 (d, 1 H, NH-Ala), 5.52 (d, 1 H, NH-Ser), 5.37 (dd, 1 H, H-4), 5.18 (dd, 1 H, H-2), 5.15 (s, 2 H, C*H_2*Ph), 5.02 (dd, 1 H, H-3), 4.8–4.66 (m, 1 H, Hα-Ala), 4.54 (d, 1 H, H-1), 4.50–3.80 (m, 11 H, CH_2CH-Fmoc, 2 Hα-Gly, 2 Hβ-Ser, Hα-Ser, H-5, H-6a, H-6b), 2.2–1.96 (4 s, 12 H, 4 Ac), 1.41 (d, 3 H, Hβ-Ala); $J_{1,2}$ 7.8, $J_{2,3}$ 10.42, $J_{3,4}$ 3.45, $J_{4,5}$ 1.16 Hz; ^{13}C NMR: δ 172.5, 170.5, 170.2, 170.0, 169.97, 169.3, 169.2 (7 ester and amide C=O), 156.1 (NHCOO), 143.8, 143.77, 141.32, 141.31 (4 quaternary aromatic carbons–Fmoc), 135.2 (quaternary aromatic carbon–CH_2Ph), 127.8, 127.14, 127.11, 125.1, 120.0 (13 aromatic tertiary carbons), 101.8 (C-1), 71.2, 70.6 (C-5, C-3), 68.93 (Cβ-Ser), 68.89 (C-2), 67.2 (*C*H_2-Fmoc), 66.98 (*C*H_2Ph), 66.87 (C-4), 61.3 (C-6), 52.3 (Cα-Ser), 50.8 (Cα-Ala), 47.1 (*C*H-Fmoc), 41.6 (Cα-Gly), 20.6, 20.54, 20.51 (4 C*Me*), 18.6 (Cβ-Ala). Anal. Calcd for $C_{44}H_{49}N_3O_{16}$: C, 60.34; H, 5.64; N, 4.80. Found: C, 60.68; H, 5.81; N, 4.78.

*N-9-Fluorenylmethoxycarbonyl-O-[2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl)-β-*D*-glucopyranosyl]-*L*-serine benzyl ester* (**21**).—Ester **21** was synthesised, similarly to **18**, from **17a,b** (152 mg, 0.24 mmol), **11** (152 mg, 0.23 mmol), and $TrClO_4$ (8 mg); reaction time, 44 h; separated by preparative TLC (5:1 $CHCl_3$–EtOAc) R_f 0.59; HPLC: t_R 17.4 min; yield, 48 mg (20%). By use of molar ratios **11**:**17a,b**:$TrClO_4$ = 1:1:0.8 and a reaction time of 16 h, the yield was 47%; oil; $[\alpha]_D^{20}$ −0.8° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz): δ 7.78 (d, 2 H, Ar-Fmoc), 7.60 (d, 2 H, Ar-Fmoc), 7.44–7.28 (m, 9 H, Ar-Fmoc, CH_2*Ph*), 5.63 (d, 1 H, NH), 5.34 (dd, 1 H, H-4′), 5.23–5.13 (m, 3 H, C*H_2*Ph, H-1), 5.12 (dd, 1 H, H-2′), 4.96 (dd, 1 H, H-3′), 4.86 (dd, 1 H, H-2), 4.56–4.35 (m, 5 H, Hα, Hβa-Ser, C*H_2*-Fmoc, H-6a), 4.47 (d, 1 H, H-1′), 4.30–4.01 (m, 5 H, C*H*-Fmoc, H-6a′, H-6b′, H-3, H-6b), 3.88–3.80 (m, 3 H, H-2, H-5′, Hβb-Ser), 3.75 (dd, 1 H, H-4), 3.52 (ddd, 1 H, H-5), 2.18–1.97 (7 s, 21 H, 7Ac); for galactose ring: $J_{1',2'}$ 7.8, $J_{2',3'}$ 10.4, $J_{3',4'}$ 3.4, $J_{5',6a'}$ 7.0, $J_{5',6b'}$ 6.5, $J_{6a',6b'}$ ~ 10 Hz; for glucose ring: $J_{1,2}$ 8, $J_{2,3}$ 9.3, $J_{3,4}$ 9.2 Hz; ^{13}C NMR: δ 170.2, 170.0, 169.9, 169.5, 169.4, 169.3, 168.9 (8 ester C=O), 155.8 (NHCOO), 143.7, 143.6, 141.3, 141.2 (4 quaternary aromatic carbons–Fmoc), 135.1 (quaternary aromatic carbon–CH_2Ph), 128.5, 128.4, 128.1, 127.7, 127.0, 124.9, 120.0 (13 tertiary aromatic carbons), 100.96 (C-1′), 100.81 (C-1), 76.0 (C-4), 72.6, 72.5, 71.4, 70.9, 70.6, 69.0 (C-2, C-3, C-5, C-2′, C-3′, C-5′), 69.4 (Cβ-Ser), 67.5, 67.0 (*C*H_2-Fmoc, *C*H_2Ph), 66.6 (C-4′), 61.8, 60.8 (C-6, C-6′), 54.5 (Cα-Ser), 47.1 (*C*H-Fmoc), 20.7, 20.69, 20.53, 20.46, 20.41 (7 C*Me*). Anal. Calcd for $C_{51}H_{57}NO_{22}$: C, 59.13; H, 5.55; N, 1.35. Found: C, 59.31; H, 5.42; N, 1.48.

O-Acetyl-N-9-fluorenylmethoxycarbonyl-serine benzyl ester (**32**).—Ester **32** was isolated from the reaction products in the synthesis of compound **19**; molar ratios (*b*); oil; yield, 13 mg (20%); TLC: R_f 0.53 (1:1 hexane–EtOAc); HPLC: t_R 11.5 min. MS(EI): M^+ 459.1686. Calcd for $C_{27}H_{25}NO_6$: 459.1682. Fragmentation: m/z 268, 221, 196, 180, 179, 178(base), 177, 176, 166, 165, 102, 91, 89, 43, 28, 18. ^{1}H NMR (250 MHz): δ 7.75 (d, 2 H, Ar-Fmoc), 7.59 (d, 2 H, Ar-Fmoc), 7.42–7.25 (m, 9 H, Ar-Fmoc, CH_2Ph), 5.60 (d, 1 H, NH), 5.22 (AB, 2 H, CH_2Ph), 4.68 (dt, 1 H, Hα-Ser), 4.51 (dd, 1 H, Hβa-Ser), 4.42 (d, 2 H, CH_2-Fmoc), 4.35 (dd, 1 H, Hβb-Ser), 4.23 (t, 1 H, CH-Fmoc), 1.95 (s, 3 H, Ac); J_{AB} 12.1, $J_{NH,H\alpha}$ 8.3, $J_{H\alpha,H\beta a}$ 3.6, $J_{H\alpha,H\beta b}$ 3.9, $J_{H\beta a,H\beta b}$ 11.4, $J_{CH,CH2}$ (Fmoc) 7.2 Hz.

References

[1] J. Montreuil, *Adv. Carbohydr. Chem. Biochem.*, 37 (1980) 157–223.

[2] H. Paulsen, *Angew. Chem.*, 102 (1990) 851–867; *Angew. Chem., Int. Ed. Engl.*, 29 (1990) 823–839.

[3] H. Paulsen, K. Adermann, G. Merz, M. Schulz, and U. Weichert, *Starch / Staerke*, 40 (1988) 465–472.

[4] H. Kunz, *Angew. Chem.*, 99 (1987) 297–311; *Angew. Chem., Int. Ed. Engl.*, 26 (1987) 294–308.

[5] H. Kunz, *Trends Glycosci. Glycotechnol.*, 4 (1992) 71–82.

[6] R.R. Schmidt, *Angew. Chem.*, 98 (1986) 213–236; *Angew. Chem., Int. Ed. Engl.*, 25 (1986) 212–235.

[7] H.G. Garg and R.W. Jeanloz, *Adv. Carbohydr. Chem. Biochem.*, 43 (1985) 135–201.

[8] J. Gigg and R. Gigg, *Top. Curr. Chem.*, 154 (1990) 77–138.

[9] K. Osamu and O. Hindsgaul, *Curr. Opin. Struct. Biol.*, 2 (1992) 674–681.

[10] A.M. Jansson, M. Meldal, and K. Bock, *J. Chem. Soc., Perkin Trans. 1*, (1992) 1699–1707.

[11] S. Peters, T. Bielfeldt, M. Meldal, K. Bock, and H. Paulsen, *J. Chem. Soc., Perkin Trans. 1*, (1992) 1163–1171.

[12] H. Paulsen and M. Brenken, *Liebigs Ann. Chem.*, (1988) 649–654.

[13] W. Kowollik, G. Janairo, and W. Voelter, *Liebigs Ann. Chem.*, (1988) 427–431.

[14] H. Kessler, M. Kottenhahn, A. Kling, and C. Kolar, *Angew. Chem.*, 99 (1987) 919–921; *Angew. Chem., Int. Ed. Engl.*, 26 (1987) 888–890.

[15] M. Hollósi, E. Kollát, I. Laczkó, K.F. Medzihradszky, J. Thurin, and L. Otvös, Jr, *Tetrahedron Lett.*, 32 (1991) 1531–1534.

[16] B. Lüning, T. Norberg, and J. Tejbrant, *Glycoconjugate J.*, 6 (1989) 5–19.

[17] L. Szabó, Yushun Li, and R. Polt, *Tetrahedron Lett.*, 32 (1991) 585–588.

[18] R. Polt, L. Szabó, J. Treiberg, Yushun Li, and V. Hruby, *J. Am. Chem. Soc.*, 114 (1992) 10249–10258.

[19] R.R. Schmidt and J. Michel, *Angew. Chem.*, 92 (1980) 763–764; *Angew. Chem., Int. Ed. Engl.*, 19 (1980) 731–732.

[20] G. Grundler and R.R. Schmidt, *Liebigs Ann. Chem.*, (1984) 1826–1847.

[21] H. Kunz and H. Waldmann, *Angew. Chem.*, 96 (1984) 49–50; *Angew. Chem., Int. Ed. Engl.*, 23 (1984) 71–72.

[22] H. Paulsen, W. Rauwald, and U. Weichert, *Liebigs Ann. Chem.*, (1988) 75–86.

[23] P. Fügedi, P.J. Garegg, H. Lönn, and T. Norberg *Glycoconjugate J.*, 4 (1987) 97–108.

[24] F. Dasgupta and P.J. Garegg, *Carbohydr. Res.*, 177 (1988) C13–C17.

[25] A.F. Bochkov and G.E. Zaikov, *Chemistry of the O-Glycosidic Bond: Formation and Cleavage*, Pergamon, Oxford, 1979, pp 82, 100, 106, 112.

[26] H. Bredereck, A. Wagner, and G. Faber, *Angew. Chem.*, 69 (1957) 438.

[27] H. Bredereck, A. Wagner, G. Faber, H. Ott, and J. Rauther, *Chem. Ber.*, 92 (1959) 1135–1139.

[28] H. Bredereck, A. Wagner, H. Kuhn, and H. Ott, *Chem. Ber.*, 93 (1960) 1201–1206.

[29] H. Bredereck, A. Wagner, D. Geissel, P. Gross, U. Hutten, and H. Ott, *Chem. Ber.*, 95 (1962) 3056–3063.

[30] A.F. Bochkov and N.K. Kochetkov, *Carbohydr. Res.*, 39 (1975) 355–357.

[31] N.K. Kochetkov, *Tetrahedron*, 43 (1987) 2389–2436.

[32] K. Barlos, P. Mamos, D. Papaioannou, S. Patrianakou, C. Sanida, and W. Schäfer, *Liebigs Ann. Chem.*, (1987) 1025–1030.

[33] L.A. Carpino and G.Y. Han, *J. Org. Chem.*, 37 (1972) 3404–3409.

[34] V.I. Betaneli, M.V. Ovchinnikov, L.V. Backinowsky, and N.K. Kochetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1979) 2751–2758; *Carbohydr. Res.*, 68 (1979) C11–C13.

[35] J. Banoub and D.R. Bundle, *Can. J. Chem.*, 57 (1979) 2085–2090.

[36] J. Banoub and D.R. Bundle, *Can. J. Chem.*, 57 (1979) 2091–2097.

[37] D.M. Andrews and P.W. Seale, *Int. J. Peptide Protein Res.*, 42 (1993) 165–170.

[38] R. Dijkman, N. Dekker, and G.H. De Haas, *Biochim. Biophys. Acta*, 1043 (1990) 67–74.

[39] K. Barlos, D. Papaioannou, and D. Theodoropoulos, *J. Org. Chem.*, 47 (1982) 1324–1326.